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Attorney Docket No.: 02307E-080710US **PATENT**

TOWNSEND and TOWNSEND and CREW LLP

By: *RLewis***IN THE UNITED STATES PATENT AND TRADEMARK OFFICE****In re application of:**

Emil A. Tanagho
Rajvir Dahiya
Tom F. Lue

Application No.: 10/052,889

Filed: January 18, 2002

For: ACELLULAR MATRIX GRAFTS:
PREPARATION AND USE

Customer No.: 20350

Confirmation No. 3329

Examiner: Prebilic, Paul B.

Technology Center/Art Unit: 3738

SUPPLEMENTAL DECLARATION
UNDER 37 C.F.R. §1.132 OF DR. EMIL A.
TANAGHO

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Emil A. Tanagho, being duly warned that willful false statements and the like
are punishable by fine or imprisonment or both (18 U.S.C. § 1001), and may jeopardize the
validity of the patent application or any patent issuing thereon, state and declare as follows:

1. All statements herein made of my own knowledge are true, and statements
made on information or belief are believed to be true and correct.

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2. The invention of the above-referenced patent application provides for the first time an organ-specific, insoluble elastic matrix graft for repair of ureter and urethra. This matrix graft is derived from donor's ureter or urethra smooth muscle tissue, is impermeable to urine, provides a scaffold for seeding of recipient's functional ureteral and urethral cells as it forms an intact framework of collagen and elastic fibers and permits recipient's cellular and muscular tissue to localize, germinate, and grow within such framework.

3. I am a named inventor on this patent application. I have read and am familiar with the contents of this patent application. In addition, I have read the Final Office Action mailed March 6, 2006, for the present application. It is my understanding that the Examiner considers my previous declaration (filed December 16, 2005) "a statement of one inventor's opinion" that is "about as valuable as anecdotal evidence," because evidence of successful treatment of only one patient was provided in the declaration. It is my further understanding that the Examiner remains unconvinced by my previous declaration because the declaration did not present quantitative and comparative data demonstrating the difference between the claimed invention and the art.

4. This supplemental declaration is provided to explain that: first, the extraordinary properties of the claimed acellular matrix graft and its successful use have been consistently demonstrated in the treatment of more than one patient; second, there can be no comparative data directly comparing the matrix of this invention and the tissue-derived material in the art, because the latter is not suitable for implantation in humans to repair damaged ureter or urethra; and third, quantitative data demonstrating the performance of the claimed matrix graft in animal experiments have been provided in references previously made of record.

5. Contrary to the Examiner's assertion, the present inventors have so far performed on at least 12 human patients surgical procedures similar to that described in my previous declaration using the claimed matrix graft of this invention. In each case, the procedure has led to dramatic improvement in patient's condition as indicated by X-ray imaging and urine flow rate measurement. Thus, the extraordinary properties and unexpected success of the

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claimed matrix graft are not merely my personal opinion; they are facts proven by a multitude of clinical studies.

6. In direct contrast with the matrix graft of this invention, which is derived from ureter or urethra smooth muscle tissue, the references by Bishopric and Goldstein teach the making of an acellular collagenous matrix derived from different tissue types, for example, heart valve and skin. The reference by Gregory teaches elastin extraction and purification, which leads to the disruption of the collagenous network of a tissue. For a graft material to be useful in ureter/urethra repair, the material must have a high level of structural integrity and flexibility, as well as water impermeability, such that the repaired tissue can perform its intended function, *i.e.*, to hold urine under a certain amount of pressure. The material produced by Bishopric, Goldstein, or Gregory does not meet such requirements because of the chosen tissue type or the loss of collagen, as tissue graft derived from heart valve or skin does not have the required elasticity and tissue without an intact collagen network does not have the required strength and structural integrity. Thus, no person of skill in the art would ever consider using the material described in the references for implantation on a human patient to repair damaged ureter or urethra tissue. The type of comparative data the Examiner has asked for simply cannot be obtained for ethical reasons.

7. I respectfully disagree with the Examiner's comments that no quantitative data were presented in my previous declaration. In fact, results of several animal experiments quantitatively illustrating the outstanding, unexpected quality of the matrix of this invention can be found in the four references named in paragraph 15 of my previous declaration. Insofar as the surgical repair of human ureter or urethra is concerned, quantitative data are not a preferred means to evaluate the effectiveness of the procedure. Because patient's overall physical condition (age, general health, *etc.*) as well as the extent and severity of tissue damage can vary significantly from individual to individual, quantitative data can provide only limited useful information. Moreover, surgical retrieval of post-implantation matrix graft is often necessary in order to obtain quantitative data for assessing the effectiveness of the matrix graft. Such retrieval, however, can be performed ethically in animals only and not in human patients.

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Emil Tanagho

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8. In summary, the matrix graft of the present invention has been shown, through the actual use in at least 12 patients, to possess extraordinary properties that simply cannot be expected from combining the teaching of the art. No comparative data can be offered because the material taught in the art is not suitable for repair of human ureter or urethra.

9. Declarant has nothing further to say.

Date:

7/24/06

By:

Emil A. Tanagho, M.D.

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